General

Guideline Title

Evidence-based guideline summary: evaluation, diagnosis, and management of facioscapulohumeral muscular dystrophy: report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology and the Practice Issues Review Panel of the American Association of Neuromuscular & Electrodiagnostic Medicine.

Bibliographic Source(s)

Tawil R, Kissel JT, Heatwole C, Pandya S, Gronseth G, Benatar M. Evidence-based guideline summary: Evaluation, diagnosis, and management of facioscapulohumeral muscular dystrophy: Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology and the Practice Issues Review Panel of the American Association of Neuromuscular & Electrodiagnostic Medicine. Neurology. 2015 Jul 28;85(4):357-64. [40 references] PubMed

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Recommendations

Major Recommendations

Definitions of the levels of the recommendations (A, B, C, U) and classification of the evidence (Class I-IV) are provided at the end of the "Major Recommendations" field.

Practice Recommendations

The recommendations below encompass 4 major areas: diagnosis, predictors of severity, surveillance for complications, and treatment.

Diagnosis of Facioscapulohumeral Muscular Dystrophy (FSHD)

Clinical Context

When clinical presentation of FSHD is typical and the inheritance pattern is consistent with autosomal dominant inheritance, clinical diagnosis is usually straightforward. If, in such circumstances, the diagnosis is genetically confirmed in a first-degree relative, genetic testing is not necessary for each affected individual. However, atypical presentations are not uncommon. In the setting of atypical or sporadic cases, genetic confirmation is important for genetic counseling, especially with the recent discovery of 2 genetically distinct forms of FSHD.

In the most common FSHD type, FSHD1, disease results from contraction of a DNA repeat sequence, termed *D4Z4 repeat*, on 1 copy of 4q35

from >10 repeats to 1–10 repeats. In addition, the contraction must occur in the presence of 1 particular (A variant) of 2 (A/B) sequence variants distal to the repeats. Available molecular testing for FSHD1, which measures only the presence of a repeat contraction on initial testing, is highly sensitive and specific. In studies that utilized strict diagnostic criteria for FSHD, determining whether a contraction occurs on an A variant genetic background does not appear to improve diagnostic specificity. However, in clinical practice, strict clinical diagnostic criteria might not be adhered to, increasing the chances of a false-positive result. In consequence, determining that a D4Z4 contraction is occurring on an A variant is warranted when the clinical presentation is atypical for FSHD. At present, commercial genetic testing in FSHD is limited to FSHD1 testing.

Recommendation

Clinicians should obtain genetic confirmation of FSHD1 in patients with atypical presentations and no first-degree relatives with genetic confirmation of the disease (Level B). The figure in the original guideline document shows the recommended FSHD molecular diagnosis decision tree.

Predictors of Severity in FSHD

Clinical Context

Factors that predict disease severity in FSHD are important for counseling patients and for screening for and managing potential complications. The D4Z4 deletion size appears to be somewhat predictive of the overall rate of disease progression. D4Z4 deletion size should be used cautiously for predicting disease progression rate in any particular individual due to other sources of variation affecting disease severity, including intrafamilial factors. Clinical experience suggests that patients with severe childhood-onset disease almost invariably have very large deletions (i.e., contracted D4Z4 allele of 10–20 kb or 1–4 repeats), suggesting a much more robust correlation between disease severity and large deletions.

Recommendation

Large D4Z4 deletion sizes (contracted D4Z4 allele of 10–20 kb) should alert the clinician that the patient is more likely to develop more significant disability and at an earlier age. Patients with large deletions are also more likely to develop symptomatic extra muscular manifestations (Level B) (see the next section, "Monitoring for Complications of FSHD").

Monitoring for Complications of FSHD

Pulmonary Complications

Clinical Context

The guideline panel's systematic review revealed that some patients with FSHD develop respiratory muscle weakness that can result in respiratory failure and need for mechanical ventilator assistance (e.g., nocturnal bilevel positive airway pressure), although this complication is uncommon. Patients with chronic respiratory failure from neuromuscular-related weakness often do not have classic symptoms of ventilatory failure (i.e., overt dyspnea). Impending respiratory failure, therefore, may begin with respiratory insufficiency mainly during sleep, resulting in excessive daytime somnolence or nonrestorative sleep. Respiratory insufficiency in patients with FSHD, therefore, may be evident only through pulmonary function testing. Respiratory failure constitutes a major source of morbidity in patients with most MD types and can severely disrupt sleeping, daily activities, and quality of life (QOL). Early intervention with noninvasive mechanical ventilation leads to improved survival and QOL.

Recommendations

Clinicians should obtain baseline pulmonary function tests on all patients with FSHD. Patients should be monitored regularly if they have abnormal baseline pulmonary function test results or any combination of severe proximal weakness, kyphoscoliosis, wheelchair dependence, or comorbid conditions that may affect ventilation (e.g., chronic obstructive pulmonary disease, cardiac disease) (Level B).

In patients who have FSHD and either (1) compromised pulmonary function studies (e.g., forced vital capacity <60%) or (2) symptoms of excessive daytime somnolence or nonrestorative sleep (e.g., frequent nocturnal arousals, morning headaches), clinicians should refer patients for pulmonary or sleep medicine consultation for consideration of nocturnal sleep monitoring or nocturnal noninvasive ventilation in order to improve QOL (Level B).

Patients with FSHD who do not get regular pulmonary function testing should be tested prior to surgical procedures requiring general anesthesia, as such testing may uncover asymptomatic respiratory compromise (Level B).

Cardiac Abnormalities

Clinical Context

The guideline panel's systematic review revealed very little evidence for structural cardiac abnormalities in FSHD. Also, data are insufficient to suggest that patients with FSHD are susceptible to cardiac arrhythmias. Routine electrocardiographic/echocardiographic testing is therefore unnecessary in patients with FSHD who are asymptomatic.

Recommendation

Patients with FSHD should be referred for cardiac evaluation if they develop overt signs or symptoms of cardiac disease (e.g., shortness of breath, chest pain, palpitations). However, routine cardiac screening is not essential in the absence of cardiac signs or symptoms (Level C).

Retinal Vascular Disease

Clinical Context

The guideline panel's systematic review suggests that symptomatic retinal vascular disease in the form of an exudative retinopathy (Coats disease) is very rare in FSHD but tends to affect patients with large deletions almost exclusively. Untreated exudative retinopathy can lead to significant visual loss, which may be prevented by early intervention.

Recommendation

Clinicians should refer patients with FSHD and large deletions (contracted D4Z4 allele of 10–20 kb) to an experienced ophthalmologist (e.g., retina specialist) for dilated indirect ophthalmoscopy (Level B). The presence and severity of retinal vascular disease at initial screening should be used to determine the frequency of subsequent monitoring (Level B).

Hearing Loss

Clinical Context

The guideline panel's systematic review shows that the available studies fail to capture the prevalence and clinical relevance of hearing loss in FSHD. In clinical practice, most patients with FSHD and hearing loss requiring the use of a hearing aid have childhood-onset FSHD with large D4Z4 deletions. Two recent studies support this clinical impression. Moreover, one of the studies suggests that hearing loss is progressive in some patients. Adults and older children are cognizant of the hearing loss onset, and therefore intervention can occur early when required. However, failure to detect hearing loss in infants and younger children may significantly delay or impair language development.

Recommendation

Clinicians should screen all young children with FSHD at diagnosis and yearly thereafter until these children start school, as hearing loss may not be present at diagnosis and can be progressive (Level B).

Pain

Clinical Context

Pain is a common complaint in FSHD and appears to be mostly musculoskeletal in origin. Pain compounding muscle weakness can have a significant impact on QOL. Physical therapists often can provide insight into the mechanism of pain in patients with weakness. Non steroidal anti-inflammatory medications are useful for acute pain, and antidepressants or antiepileptics for chronic musculoskeletal pain.

Recommendation

Treating physicians should routinely inquire about pain in patients with FSHD. Referral for a physical therapy evaluation may prove helpful as an initial nonpharmacologic intervention. In patients with persistent pain and no contraindications, a trial of nonsteroidal anti-inflammatory medications is appropriate for acute pain and antidepressants or antiepileptics for chronic pain (Level B).

Treatment of FSHD

Pharmacologic Interventions

Clinical Context

As of this writing, no evidence exists for any effective pharmacologic interventions that improve strength or slow disease progression in FSHD. Randomized, controlled trials of albuterol were negative. Uncontrolled, open-label trials of corticosteroid and diltiazem showed no benefit. A controlled early phase II study of MYO-029, a myostatin inhibitor, also failed to show benefit.

Recommendation

In patients with FSHD, clinicians should not prescribe albuterol, corticosteroid, or diltiazem for improving strength (Level B).

Surgical Scapular Fixation

Clinical Context

In patients with FSHD, limited shoulder range of motion due to periscapular muscle weakness is a major source of functional limitation. Moreover, in many patients, bedside manual scapular fixation can result in significant improvement in shoulder range of motion. Postoperative complications are infrequent but include hemothorax or pneumothorax, pain, infection, nonunion, and reduced lung capacity. Scapular fixation appears to be generally safe and may be effective for improving shoulder range of motion.

Recommendation

Surgical scapular fixation might be offered cautiously to selected patients after careful consideration of the overall muscle impairment in the involved arm, assessment of potential gain in range of motion by manual fixation of the scapula, the patient's rate of disease progression, and the potential adverse consequences of surgery and prolonged postsurgical bracing (Level C).

Aerobic Exercise

Clinical Context

Aerobic exercise in FSHD appears to be safe and potentially beneficial, as has been shown in many other muscle diseases. Aerobic fitness is important for overall health. To minimize injury from falls or overuse, the type of aerobic exercise should be tailored to the patient's particular distribution of weakness. For example, a stationary bicycle rather than a treadmill should be recommended for patients with leg weakness. Although no data exist to suggest that strength training is detrimental in FSHD, further research is needed to determine whether such strength training will result in clinically meaningful long-term functional improvement.

Recommendations

Clinicians might encourage patients with FSHD to engage in low-intensity aerobic exercise. An experienced physical therapist can help guide development of individualized exercise programs. Clinicians might also use the practical physical activities guidelines for individuals with disabilities, provided by the US Department of Health and Human Services, when counseling patients about aerobic exercise (Level C).

In patients interested in strength training, clinicians may refer patients to physical therapists to establish a safe exercise program using appropriate low/ medium weights/resistance that takes into consideration the patients' physical limitations (Level C).

Definitions

American Academy of Neurology (AAN) Rules for Classification of Evidence for Risk of Bias

For Questions Related to Screening (Yield)

Class I

- Study of a cohort of patients at risk for the outcome from a defined geographic area (i.e., population based)
- The outcome is objective
- Also required:
    a. Inclusion criteria defined
    b. At least 80% of patients undergo the screening of interest

Class II

- A non-population-based, nonclinical cohort (e.g., mailing list, volunteer panel) or a general medical, neurology clinic/center without a specialized interest in the outcome. Study meets criteria a b (see Class I)
- The outcome is objective

Class III

A referral cohort from a center with a potential specialized interest in the outcome

Class IV

- Did not include persons at risk for the outcome
- Did not statistically sample patients, or patients specifically selected for inclusion by outcome
- Undefined or unaccepted screening procedure or outcome measure
- No measure of frequency or statistical precision calculable

For Questions Related to Prognostic Accuracy

Class I

- Cohort survey with prospective data collection
- Includes a broad spectrum of persons at risk for developing the outcome
- Outcome measurement is objective or determined without knowledge of risk factor status
- Also required:
    a. Inclusion criteria defined
    b. At least 80% of enrolled subjects have both the risk factor and outcome measured

Class II

- Cohort study with retrospective data collection or case-control study. Study meets criteria a and b (see Class I)
- Includes a broad spectrum of persons with and without the risk factor and the outcome
- The presence of the risk factor and outcome are determined objectively or without knowledge of one another

Class III

- Cohort or case-control study
- Narrow spectrum of persons with or without the disease
- The presence of the risk factor and outcome are determined objectively, without knowledge of the other or by different investigators

Class IV

- Did not include persons at risk for the outcome
- Did not include patients with and without the risk factor
- Undefined or unaccepted measures of risk factor or outcomes
- No measures of association or statistical precision presented or calculable

For Questions Related to Therapeutic Intervention

Class I

- Randomized, controlled clinical trial in a representative population
- Masked or objective outcome assessment
- Relevant baseline characteristics are presented and substantially equivalent between treatment groups, or there is appropriate statistical adjustment for differences
- Also required:
    a. Concealed allocation
    b. Primary outcome(s) clearly defined
    c. Exclusion/inclusion criteria clearly defined
    d. Adequate accounting for dropouts (with at least 80% of enrolled subjects completing the study) and crossovers with numbers sufficiently low to have minimal potential for bias
    e. For noninferiority or equivalence trials claiming to prove efficacy for one or both drugs, the following are also required*:
        1. The authors explicitly state the clinically meaningful difference to be excluded by defining the threshold for equivalence or noninferiority
        2. The standard treatment used in the study is substantially similar to that used in previous studies establishing efficacy of the standard treatment (e.g., for a drug, the mode of administration, dose, and dosage adjustments are similar to those previously shown to be effective
        3. The inclusion and exclusion criteria for patient selection and the outcomes of patients on the standard treatment are comparable to those of previous studies establishing efficacy of the standard treatment

4. The interpretation of the study results is based on a per-protocol analysis that accounts for dropouts or crossovers

Class II

- Cohort study meeting criteria a–e above or a randomized, controlled trial that lacks one or two criteria b–e
- All relevant baseline characteristics are presented and substantially equivalent among treatment groups, or there is appropriate statistical adjustment for differences
- Masked or objective outcome assessment

Class III

- Controlled studies (including studies with external controls such as well-defined natural history controls)
- A description of major confounding differences between treatment groups that could affect outcome**
- Outcome assessment masked, objective, or performed by someone who is not a member of the treatment team

Class IV

- Did not include patients with the disease
- Did not include patients receiving different interventions
- Undefined or unaccepted interventions or outcome measures
- No measures of effectiveness or statistical precision presented or calculable

*Numbers 1–3 in Class Ie are required for Class II in equivalence trials. If any one of the three is missing, the class is automatically downgraded to Class III.

**Objective outcome measurement: an outcome measure that is unlikely to be affected by an observer's (patient, treating physician, investigator) expectation or bias (e.g., blood tests, administrative outcome data)

Assigning a Level of Strength to the Recommendation

When there is sufficient evidence to support an inference for the use of an intervention (i.e., the balance of benefits and harms favors the intervention), the author panel assigns one of three recommendation designations: A, B, or C. Each designation corresponds to a helping verb that denotes the level of strength of the recommendation. Level A is the strongest recommendation level and is denoted by the use of the helping verb *must*. *Must* recommendations are rare, as they are based on high confidence in the evidence and require both a high magnitude of benefit and low risk. Level B corresponds to the helping verb should. Should recommendations tend to be more common, as the requirements are less stringent but still based on the evidence and benefit–risk profile. Finally, Level C corresponds to the helping verb may or might. *May* and *might* recommendations represent the lowest allowable recommendation level the American Academy of Neurology (AAN considers useful within the scope of clinical practice and can accommodate the highest degree of practice variation.

Level A denotes a practice recommendation that "must" be done. In almost all circumstances, adherence to the recommendation will improve health-related outcomes. A Level B indicates a recommendation that "should" be done. In most circumstances, adherence to the recommendation will likely improve health-related outcomes. A Level C represents a recommendation that "might" be done. In some circumstances, adherence to the recommendation might improve health-related outcomes.

When there is insufficient evidence to support an inference for the use of an intervention (i.e., the balance of benefits and harms is unknown) a Level U or Level R designation is appropriate.

A Level U indicates that the available evidence is insufficient to support or refute the efficacy of an intervention. A Level R is assigned when the balance of benefits and harms is unknown and the intervention is known to be expensive or have important risks. A Level R designates that the intervention should not be used outside of a research setting. Non-evidence-based factors that need to be transparently and systematically considered when formulating recommendations include the following:

- The relative value of the benefit as compared with the risk; this is derived from consideration of:
    - The importance to patients of the health related-outcomes (both benefits and harms)
    - The size of the intervention's effect
    - The risk of harm of the intervention (i.e., tolerability and safety)
- The feasibility of complying with the intervention (e.g., the intervention's availability)
- The cost of the intervention
- The expected variation in patient preferences relative to the risks, burdens, and benefits of the intervention

Clinical Algorithm(s)

An algorithm titled "Recommended Diagnostic Flowchart for Facioscapulohumeral Muscular Dystrophy" is provided in the original guideline document.

Scope

Disease/Condition(s)

Facioscapulohumeral muscular dystrophy (FSHD)

Note: This guideline focuses exclusively on FSHD. Duchenne muscular dystrophy (MD) and myotonic dystrophy will be discussed in forthcoming guidelines; limb-girdle MD and congenital MD are addressed in separate guidelines.

Guideline Category

Diagnosis

Evaluation

Management

Treatment

Clinical Specialty

Neurology

Intended Users

Physicians

Guideline Objective(s)

To develop recommendations for the evaluation, diagnosis, prognostication, and treatment of facioscapulohumeral muscular dystrophy (FSHD) from a systematic review and analysis of the evidence

Target Population

Patients with clinically defined facioscapulohumeral muscular dystrophy (FSHD)

Interventions and Practices Considered

1. Diagnosis of facioscapulohumeral muscular dystrophy type 1 (FSHD1)
    - Genetic confirmation
    - Indication of large D4Z4 deletion sizes
2. Monitoring complications
    - Baseline pulmonary function tests
    - Cardiac evaluation
    - Dilated indirect ophthalmoscopy (retina vascular disease)
    - Screening for hearing loss

    - Management of pain (physical therapy or nonsteroidal anti-inflammatories/antidepressants/antiepileptics)
3. Treatment of FSHD
    - Surgical scapular fixation (offered cautiously)
    - Aerobic exercise
    - Albuterol, corticosteroid, or diltiazem (not recommended)

Major Outcomes Considered

- Efficacy and safety of the treatments
- Complications
    - Respiratory abnormalities
    - Cardiac abnormalities
    - Retinal disease
    - Hearing loss
    - Pain
- Quality of life

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

In July 2010, the Guideline Development, Dissemination, and Implementation Subcommittee (GDDI) of the American Academy of Neurology (AAN) and the Practice Issues Review Panel (PIRP) of the American Association of the Neuromuscular & Electrodiagnostic Medicine (AANEM) convened a panel of clinicians with expertise in facioscapulohumeral muscular dystrophy (FSHD) (see Appendices e-1 and e-2 in the FSHD Guideline [see the "Availability of Companion Documents" field] for a listing of the members of the AAN GDDI and AANEM PIRP). In accordance with the processes outlined in the 2004 and 2011 AAN guideline development manuals, the panel searched the Medline, EMBASE, Cochrane, and Scopus databases from 1948 to October 2012 for relevant peer-reviewed articles in humans and in all languages (see Appendix e-3 in the FSHD Guideline for search strategies).

The guideline addresses the following practical issues related to FSHD (reflective only of evidence relevant to FSHD1; no large FSHD2 clinical studies exist):

1. For patients with clinically defined FSHD (as determined by explicitly stated clinical criteria substantially similar to the consortium criteria), how often does D4Z4 contraction on 4q35 confirm the diagnosis of FSHD (irrespective of its occurrence on an allele A)? For individuals who do not have FSHD, how often is a D4Z4 contraction on 4q35 found? For individuals who do not have FSHD, how often is a D4Z4 contraction on 4q35 on allele A found?
2. Which factors are associated with or predict loss of clinically meaningful milestones (e.g., loss of independent ambulation)?
3. How frequent are respiratory abnormalities, cardiac abnormalities, retinal disease, hearing loss, and pain?
4. Do interventions (as compared with no intervention) improve patient relevant outcomes? Are there features that identify patients who are more or less likely to improve with a specific intervention?

Selected articles contained information relevant to the 4 questions posed above and had acceptable study designs, including randomized, controlled trials; cohort studies; case-control studies; and case series. Reviews and meta-analyses were excluded, as were studies with 6 or fewer participants for studies of FSHD complications and prognosis, fewer than 9 participants for genetic screening, and fewer than 5 participants for treatment. Also excluded were studies not relevant to the clinical questions, studies including participants who had unrelated diseases or were outside of the study population, and articles that were not peer reviewed.

Number of Source Documents

The initial search yielded 977 abstracts. Of those, 176 were obtained for full-text review. Each of the 176 articles was reviewed by 2 panel members working independently of each other. A total of 94 articles were selected for inclusion in the analysis, and of those, 76 articles were selected for evidence rating. An updated literature search completed in January 2014 identified an additional 12 potentially relevant articles, 4 of which were selected for evidence rating.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

American Academy of Neurology (AAN) Rules for Classification of Evidence for Risk of Bias

For Questions Related to Screening (Yield)

Class I

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- The outcome is objective
- Also required:
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    b. At least 80% of patients undergo the screening of interest

Class II

- A non-population-based, nonclinical cohort (e.g., mailing list, volunteer panel) or a general medical, neurology clinic/center without a specialized interest in the outcome. Study meets criteria a b (see Class I)
- The outcome is objective

Class III

A referral cohort from a center with a potential specialized interest in the outcome

Class IV

- Did not include persons at risk for the outcome
- Did not statistically sample patients, or patients specifically selected for inclusion by outcome
- Undefined or unaccepted screening procedure or outcome measure
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- Cohort survey with prospective data collection
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- Cohort study with retrospective data collection or case-control study. Study meets criteria a and b (see Class I)
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- The presence of the risk factor and outcome are determined objectively or without knowledge of one another

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For Questions Related to Therapeutic Intervention

Class I

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    b. Primary outcome(s) clearly defined
    c. Exclusion/inclusion criteria clearly defined
    d. Adequate accounting for dropouts (with at least 80% of enrolled subjects completing the study) and crossovers with numbers sufficiently low to have minimal potential for bias
    e. For noninferiority or equivalence trials claiming to prove efficacy for one or both drugs, the following are also required*:
        1. The authors explicitly state the clinically meaningful difference to be excluded by defining the threshold for equivalence or noninferiority
        2. The standard treatment used in the study is substantially similar to that used in previous studies establishing efficacy of the standard treatment (e.g., for a drug, the mode of administration, dose, and dosage adjustments are similar to those previously shown to be effective)
        3. The inclusion and exclusion criteria for patient selection and the outcomes of patients on the standard treatment are comparable to those of previous studies establishing efficacy of the standard treatment
        4. The interpretation of the study results is based on a per-protocol analysis that accounts for dropouts or crossovers

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- Masked or objective outcome assessment

Class III

- Controlled studies (including studies with external controls such as well-defined natural history controls)
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**Objective outcome measurement: an outcome measure that is unlikely to be affected by an observer's (patient, treating physician, investigator) expectation or bias (e.g., blood tests, administrative outcome data)

Methods Used to Analyze the Evidence

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Each of the 76 articles was rated by 2 panel members using the American Academy of Neurology (AAN) criteria for classification of screening, prognostic, and treatment articles (see the "Rating Scheme for the Strength of the Evidence" field).

Methods Used to Formulate the Recommendations

Expert Consensus (Delphi)

Description of Methods Used to Formulate the Recommendations

The methods used to develop this guideline are detailed in the FSHD Guideline (see the "Availability of Companion Documents" field). In brief, the American Academy of Neurology (AAN) convened an author panel of clinicians with facioscapulohumeral muscular dystrophy (FSHD) expertise. The panel systematically reviewed the evidence relevant to the posed questions according to the processes described in the 2004 and 2011 AAN process manuals. The panel formulated practice recommendations based on the evidence systematically reviewed, stipulated axiomatic principles of care, strong evidence from closely related conditions, and judgments regarding risk benefit and patient preferences.

The panel formulated a rationale for recommendations based on the evidence systematically reviewed and stipulated axiomatic principles of care. This rationale is explained in a section that precedes each set of recommendations. From this rationale, corresponding actionable recommendations were inferred. The level of obligation of the recommendations was assigned using a modified Delphi process that considered the following prespecified domains: the confidence in the evidence systematically reviewed, the acceptability of axiomatic principles of care, the strength of indirect evidence, and the relative magnitude of benefit to harm. Additional factors explicitly considered by the panel that could modify the level of obligation include judgments regarding the importance of outcomes, cost of compliance with the recommendation relative to benefit, the availability of the intervention, and anticipated variations in patients' preferences. The prespecified rules for determining the final level of obligation from these domains are indicated in Appendix e-5 in the FSHD Guideline. The level of obligation was indicated using standard modal operators. *Must* corresponds to *Level A*, very strong recommendations; *should* to *Level B*, strong recommendations; and *might* to *Level C*, weak recommendations. The panel members' judgments supporting the levels of obligation are indicated in Appendix e-6 of the FSHD Guideline.

Rating Scheme for the Strength of the Recommendations

Assigning a Level of Strength to the Recommendation

When there is sufficient evidence to support an inference for the use of an intervention (i.e., the balance of benefits and harms favors the intervention), the author panel assigns one of three recommendation designations: A, B, or C. Each designation corresponds to a helping verb that denotes the level of strength of the recommendation. Level A is the strongest recommendation level and is denoted by the use of the helping verb *must*. *Must* recommendations are rare, as they are based on high confidence in the evidence and require both a high magnitude of benefit and low risk. Level B corresponds to the helping verb should. Should recommendations tend to be more common, as the requirements are less stringent but still based on the evidence and benefit–risk profile. Finally, Level C corresponds to the helping verb may or might. *May* and *might* recommendations represent the lowest allowable recommendation level the American Academy of Neurology (AAN) considers useful within the scope of clinical practice and can accommodate the highest degree of practice variation.

Level A denotes a practice recommendation that "must" be done. In almost all circumstances, adherence to the recommendation will improve health-related outcomes. A Level B indicates a recommendation that "should" be done. In most circumstances, adherence to the recommendation will likely improve health-related outcomes. A Level C represents a recommendation that "might" be done. In some circumstances, adherence to the recommendation might improve health-related outcomes.

When there is insufficient evidence to support an inference for the use of an intervention (i.e., the balance of benefits and harms is unknown) a Level U or Level R designation is appropriate.

A Level U indicates that the available evidence is insufficient to support or refute the efficacy of an intervention. A Level R is assigned when the balance of benefits and harms is unknown and the intervention is known to be expensive or have important risks. A Level R designates that the intervention should not be used outside of a research setting. Non-evidence-based factors that need to be transparently and systematically considered when formulating recommendations include the following:

- The relative value of the benefit as compared with the risk; this is derived from consideration of:
  - The importance to patients of the health related-outcomes (both benefits and harms)
  - The size of the intervention's effect
  - The risk of harm of the intervention (i.e., tolerability and safety)
- The feasibility of complying with the intervention (e.g., the intervention's availability)
- The cost of the intervention
- The expected variation in patient preferences relative to the risks, burdens, and benefits of the intervention

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

Drafts of the guideline have been reviewed by at least 3 American Academy of Neurology (AAN) committees, at least 1 American Academy of Neuromuscular & Electrodiagnostic Medicine (AANEM) committee, a network of neurologists, *Neurology*® peer reviewers, and representatives from related fields.

The guideline was approved by the Guideline Development, Dissemination, and Implementation Subcommittee (GDDI) on July 23, 2014; by the AAN Practice Committee on October 20, 2014; by the AANEM Board of Directors on April 13, 2015; and by the AANI Board of Directors on March 24, 2015.

The guideline was endorsed by the FSH Society on December 18, 2014.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate diagnosis and treatment of patients with facioscapulohumeral muscular dystrophy (FSMD)

Potential Harms

- Potential adverse consequences of surgical scapular fixation and prolonged postsurgical bracing
- To minimize injury from falls or overuse, the type of aerobic exercise should be tailored to the patient's particular distribution of weakness.

Qualifying Statements

Qualifying Statements

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Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Clinical Algorithm

Patient Resources

Quick Reference Guides/Physician Guides

Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

Staying Healthy

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

Tawil R, Kissel JT, Heatwole C, Pandya S, Gronseth G, Benatar M. Evidence-based guideline summary: Evaluation, diagnosis, and management of facioscapulohumeral muscular dystrophy: Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology and the Practice Issues Review Panel of the American Association of Neuromuscular & Electrodiagnostic Medicine. Neurology. 2015 Jul 28;85(4):357-64. [40 references] PubMed

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

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Guideline Developer(s)

American Academy of Neurology - Medical Specialty Society

American Association of Neuromuscular and Electrodiagnostic Medicine - Medical Specialty Society

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Guideline Committee

Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology and the Practice Issues Review Panel of the American Association of Neuromuscular & Electrodiagnostic Medicine

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Financial Disclosures/Conflicts of Interest

Conflict of Interest

The American Academy of Neurology (AAN) and American Association of Neuromuscular & Electrodiagnostic Medicine (AANEM) are committed to producing independent, critical, and truthful clinical practice guidelines (CPGs). Significant efforts are made to minimize the potential for conflicts of interest to influence the recommendations of this CPG. To the extent possible, the AAN and AANEM keep separate those who have a financial stake in the success or failure of the products appraised in the CPGs and the developers of the guidelines. Conflict of interest forms were obtained from all authors and reviewed by an oversight committee prior to project initiation. AAN and AANEM limit the participation of authors with substantial conflicts of interest. The AAN and AANEM forbid commercial participation in, or funding of, guideline projects. Drafts of the guideline have been reviewed by at least 3 AAN committees, at least 1 AANEM committee, a network of neurologists, *Neurology*® peer reviewers, and representatives from related fields. The AAN Guideline Author Conflict of Interest Policy can be viewed at www.aan.com. For complete information on this process, access the 2004 AAN process manual.

Disclosures

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Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

A list of American Academy of Neurology (AAN) guidelines, along with a link to this guideline, is available from the AAN Web site.

Availability of Companion Documents

The following are available:

- Evidence-based guideline summary: evaluation, diagnosis, and management of facioscapulohumeral muscular dystrophy. Data supplement (FSHD Guideline, e-references). St. Paul (MN): American Academy of Neurology; 2015. Available from the Neurology Journal Web site.
- Evidence-based guideline summary: evaluation, diagnosis, and management of facioscapulohumeral muscular dystrophy. Podcast. St. Paul (MN): American Academy of Neurology; 2015. Available from the Neurology Journal Web site.
- Evaluation, diagnosis, and management of facioscapulohumeral muscular dystrophy. Summary of evidence-based guideline for clinicians. St. Paul (MN): American Academy of Neurology; 2015. 3 p. Available from the American Academy of Neurology (AAN) Web site.
- AAN guideline development process [online]. St. Paul (MN): American Academy of Neurology. Available from the AAN Web site.

Patient Resources

The following is available:

- Facioscapulohumeral muscular dystrophy. Summary of evidence-based guideline for patients and their families. St. Paul (MN): American Academy of Neurology; 2015. 5 p. Available from the American Academy of Neurology (AAN) Web site .

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC Status

This NGC summary was completed by ECRI Institute on October 7, 2015. The information was not verified by the guideline developer.

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